Enzyme's structure reveals basis for head, sex organ deformities

August 19 2011

Scientists this month reported the molecular structural basis for severe head deformities and ambiguous sex organs in babies born with Antley-Bixler syndrome accompanied by an enzyme deficiency.

The team, composed of researchers from The University of Texas Health Science Center San Antonio, the Medical College of Wisconsin and Charles University in Prague, solved the atomic structure of this human enzyme with an impressive name — NADPH-cytochrome P450 reductase, abbreviated CYPOR.

The group is the first to visualize and depict the structure of the human version of CYPOR. The scientists also reported the structure of two mutations of human CYPOR that result in congenital deformities.

"Human syndromes are caused by the deficiency of this enzyme," said Bettie Sue Masters, Ph.D., D.Sc., M.D. (Hon.), professor of biochemistry and the Robert A. Welch Foundation Distinguished Professor in Chemistry at the UT Health Science Center. "The two mutations that we characterized are responsible for severe craniofacial and steroid-production defects in humans, the latter leading to sexual ambiguities."

In the body, steroids are produced for many important functions. In CYPOR deficiency, these steroidal malfunctions are related to deformed sexual organs and other defects.

The structural basis for human CYPOR deficiency is described in the Aug. 4 edition of *Proceedings of the National Academy of Sciences.*

In previously published research from Dr. Masters' laboratory, addition of a riboflavin (vitamin B2) derivative reversed the defects in the mutated enzymes; this is because the vitamin makes this particular enzyme work, producing metabolites. Metabolites are the products of enzyme-generated reactions. This reversal of CYPOR defects by a riboflavin derivative is yet to be investigated in animals or humans. Foods such as liver, herbs, almonds, wheat bran, fish and cheese are rich in riboflavin.

Knowing the molecular structure of CYPOR has proved that riboflavin therapy is worth attempting, Dr. Masters said. As demonstrated by this structure, CYPOR dysfunction in patients harboring these particular mutations may possibly be prevented by riboflavin therapy within the womb, if predicted before birth, or rescued after birth in less severe cases, the authors wrote in the Aug. 4 publication.

Provided by University of Texas Health Science Center at San Antonio